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THE EVALUATION OF NUTRITIONAL STATUS DISORDERS AS A STATE OF OVERWEIGHT AND HYPERLIPIDEMIA IN CHILDREN WITH CANCER

OCENA STANU ODŻYWIENIA ORAZ PARAMETRÓW GOSPODARKI LIPIDOWEJ U DZIECI LECZONYCH Z POWODU CHOROBY NOWOTWOROWEJ

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S u m m a r y

A i m   o f   s t u d y . The assessment of nutritional status with a special attention towards overweight by anthropometric measurements and biochemical parameters of lipids in children with cancer.

M a t e r i a l   a n d   m e t h o d s . In a retrospective group data of 122 patients' treatment history were analyzed. The patients were treated in our hospital in previous years and their weight and height were studied. In a prospective group 62 newly diagnosed children with cancer were examined. The additional anthropometric measurements were included in the research like skinfolds thickness and middle arm circumference and biochemical lipids date were taken. The data were analyzed three times: at the diagnosis, during the oncological treatment and after the intensive chemotherapy.

R e s u l t s . In a retrospective group, after the oncological treatment the number of children with overweight increased: M/W>90 ile 6.6%, BMI >90 ile 6.6%, %IBW above 110% 25.5%, Cole'a index above 110% 21.3% , whereas the number of children with height > 90 ile decreased to 6.6%. At the beginning, in a prospective group the number of children with overweight was three times higher-11.3%. 26.2% patients had abnormal level of triglicerydes at diagnosis and 30.4% after treatment. Above 50% of patients had abnormal level of HDL cholesterol during the whole treatment.

C o n c l u s i o n s . Children with cancer belong to the group of risk for obesity and hyperlipidemia during the oncological treatment and it may impact on treatment and outcomes and also have serious medical consequence to the health state in future.

S t r e s z c z e n i e

Głównym celem prowadzonych badań była ocena stanu odżywienia ze szczególnym uwzględnieniem parametrów antropometrycznych oraz stężenia lipidów u dzieci leczonych z powodu choroby nowotworowej

M a t e r i a ł   i   m e t o d y . Ocenie retrospektywnej poddano dane uzyskane podczas hospitalizacji 122 pacjentów leczonych w Klinice Pediatrii Hematologii i Onkologii Collegium Medicum Uniwersytetu Mikołaja Kopernika w Toruniu. Badanie poszerzono o ocenę prospektywną 62 dzieci z rozpoznaniem choroby nowotworowej. Badania

antropometryczne obejmowały pomiar fału skórnego oraz obwód ramienia, a ponadto przeprowadzono ocenę parametrów lipidowych w momencie postawienia diagnozy, w trakcie leczenia onkologicznego oraz po zakończeniu intensywnej chemioterapii.

W y n i k i . W grupie poddanej ocenie retrospektywnej, po leczeniu onkologicznym liczba dzieci z nadwagą wzrosła: M/W> 90 percentyla – 6,6%, BMI> 90% percentyla – 6,6%, powyżej 110% ICC – 25,5%, współczynnik Cole'a powyżej 110% – 21,3%, podczas gdy liczba dzieci ze wzrostem > 90

percentyla zmniejszyła się do 6,6%. Na początku leczenia, w grupie ocenianej prospektywnie liczba dzieci z nadwagą była trzy razy wyższa i wyniosła 11,3%. U 26,2% pacjentów obserwowano nieprawidłowe stężenie trójglicerydów na początku badania i u 30,4% po leczeniu. Ponad 50% pacjentów miało nieprawidłowe stężenia cholesterolu HDL podczas całego leczenia.

W n i o s k i . Dzieci leczone z powodu choroby nowo-tworowej należą do grupy podwyższonego ryzyka otyłości i hiperlipemii w czasie leczenia onkologicznego, co może wpływać na leczenie i rokowanie nie tylko krótkoterminowe, ale także odległe.

Key words: cancer in children, obesity, hyperlipidemia
Słowa kluczowe: choroba nowotworowa u dzieci, otyłość, hiperlipidemia

Abbreviations
MAC – middle arm circumference
TSFT – triceps skinfold thickness
SSFT – scapular skinfold thickness
ASFT – abdominal skinfold thickness

INTRODUCTION

The disorder of nutritional status, usually in the form of malnutrition, is often observed among in pediatric oncological patients. In the developed countries there is also a growing number of overweight patients within this group. The published reports show the problem of obesity after oncological treatment, especially among children with acute lymphoblastic leukemia. There are more and more reports on the negative impact of obesity in children on the length and quality of life among long-term pediatric cancer survivors. Also the problem of bioavailability and distribution of chemotherapy is reported within this group of patients, which may affect the effectiveness of the treatment [1-3].There are also reports about the connection between the atherosclerotic lipids disorders and diabetes or cardiovascular diseases [3-7]. The mechanism of growing lipids disorder is multifactorial with possible unfavorable impact of cancer disease and particular applied treatment.

Measuring the thickness of skinfolds thickness is a simple test helping to estimate the amount of fat tissue. The subcutaneous tissue is the first energetic reserve for organisms in the state of underfeeding or the growing loss. The local changes reflect the constitutional status, because more than a half of the fat is located in the subcutaneous tissue.

MATERIALS AND METHODS

Two groups of patients took part in the study. In the retrospective group (A) there were 122 patients at the age of 0-18, undergoing clinical oncological treatment in 2002-2008. There was the largest group of patients with acute leukemia (56 children), mostly with acute lymphoblastic leukemia, then with solid tumors (34 children) and treated due to lymphoma (32 children).

In the prospective group (B) there were 62 children at the age of 0-18 with newly diagnosed cancer, undergoing clinical treatment in 2008-2010. In the largest group there were patients with solid tumors (25 children), then patients with acute leukemia (23 children), in majority with acute lymphoblastic leukemia and 14 children undergoing treatment due to lymphoma. The assessment of the nutrition status was done 3 times: at diagnosis, half way of treatment and after the treatment was finished. In the retrospective group (A) body weight and height were measured, and such indices as BMI, Cole's, % IBW were calculated using the following formula: BMI as the weight in kilograms to height in squared meters, % IBW as percentage of the ideal weight, Cole's index as quotient of current and standard body mass index. In the prospective group (B) additional anthropometric measurements such as triceps, scapular and abdominal skinfolds thickness and the middle arm circumference were included. The biochemical lipids data were also taken: total cholesterol, HDL and LDL fractions and triglycerides.

The data were analyzed in terms of reference growth charts of Polish children population.

The Bioethics Committee at Collegium Medicum in Bydgoszcz of Nicolaus Copernicus University in Torun provided consent for conducting this experiment (KB/412/2008).

The results over 90th percentile for anthropometric measurements and 110% in %IBW and Cole's index were considered as abnormal and treated as overweight.

The statistical analysis was done with statistical computer programme Statistica 9.1 of StartSoft company. The analysis of the correlation of qualitative variables was done with the help of test X2. P<0.05 was assumed as statistically important.

RESULTS

In group A, at diagnosis, most of the parameters showed up to 10% of children above normal range, so more than 90 percentiles or 110 % for the IBW index and Cole's one. During the intensive treatment most of those indices showed the decrease in the number of children, and after the therapy all the indices, except height index, showed more percent of children than at diagnosis (table I).

In group B, 10-20 % of children, at diagnosis, showed indices, based on the weight and height, above 90 percentiles or more than 110% of the normal range, which indicated overweight. The percentage of children with weight over 90 percentiles at diagnosis was almost three times higher in group B than in group A. The percentage of children with weight and height more than 90 percentiles after treatment was smaller than at diagnosis.

Table I. *The number of patients N(%) with parameters and anthropometric indices over 90 percentiles or more than 110% of normal range for IBW and Cole's index in group A - retrospective study group of 122 patients and group B- prospective study group of 62 patients.*

Number of patients (n)	Order of assessment	Weight n (%)	Height n (%)	Weight for height index n (%)	BMI index n (%)	% IBW n (%)	Cole's index n (%)
122	at diagnosis	5 4.1	18 14.8	5 4.1	5 4.1	17 13.9	13 10.7
122	during treatment	4 3.3	9 7.4	4 3.3	4 3.3	13 10.7	18 14.8
122	after treatment	6 4.9	8 6.6	8 6.6	8 6.6	31 25.4	26 21.3
62	at diagnosis	7 11.3	7 11.3	4 6.4	8 12.9	11 17.7	13 21.0
62	during treatment	4 6.5	3 4.8	5 8.1	6 9.7	12 19.4	13 21.0
62	after treatment	5 8.1	3 4.8	8 12.9	7 11.3	18 29.0	19 30.6

Table II. *The number of patients N(%) with lipid disorders and additional anthropometric measurements over 90 percentiles in prospective group (B)*

Number of patients (n)	Order of assessment	Triglycerides >150 mg/dL n (%)	Total cholesterol >200 mg/dL n (%)	HDL cholesterol ≤40 mg/dL n (%)	LDL cholesterol ≥130 mg/dL n (%)
62	at diagnosis	16 26.2	9 14.6	41 67.2	8 13.3
62	during treatment	13 20.8	5 8.5	42 73.7	8 14.0
62	after treatment	17 30.4	4 6.8	38 66.7	6 11.1

The lipid parameters and additional anthropometric measurements in the prospective study group B.

The abnormal concentration of cholesterol HDL below 40 mg/dl was observed at 67% of children, higher level of triglycerides over 150 mg% in 26% of children – in both cases with the prevalence in patients with leukemia. In 13% percent of children higher level of cholesterol LDL 130mg% was detected, and 14% of patients had the higher level of total cholesterol >200mg%. Lipid disorders were observed at similar level also after the intensive treatment. It was a bit lower in children with higher level of total cholesterol and LDL fraction (table II).

Additional measurements of skinfolds thickness increased up to 30% the number of children, who had these parameters over 90 percentiles at diagnosis. The number of children with skinfolds thickness over 90 percentiles increased during and after treatment.

The evaluation of the relation between mathematical indices based on height and weight measurements and anthropometric parameters that were taken at the same time showed that there was a statistically important correlation in every case between %IBW and Cole's index and anthropometric parameters, and between BMI index and the middle arm circumference, the triceps and scapular skinfold thickness.

DISCUSSION

Since the 80s there have been lots of reports concerning overweight and obesity among children after oncological treatment, especially in acute lymphoblastic leukemia. The number of survivors with overweight ranges from 11 to 57% , which depends on the definition of overweight taken into account and also on the time of measurement [1, 2].

In our own study in the retrospective group there were 4.1% of overweight children at diagnosis, and not more than 6.5 % in prospective assessment. After intensive chemotherapy weight/height index more than 90 percentile in the retrospective group was still low – 6.6%, and in prospective group it was 12.9%.

Comparing the results of both examinations we observe that the number of overweight

children was higher in 2008-2010 than in 2002-2008, but still lower than data based on research done on the population of healthy Polish children and teenagers 1-18 years old in 2000 by the Institute of Food and Feeding in which weight/height index was 24.4% [8, 9, 10].

BMI index also indicated less frequent overweight in oncological patients in comparison to the population of healthy children. In the study of frequency of occurrence of overweight and obesity on the basis of Institute of Mother and Child's BMI charts, published in 2002, in the group of children at the age of 7-9, the occurrence of overweight was reported among 20.9% of children. In our own research BMI over 90 percentiles at diagnosis occurred in 4.1% of children in the retrospective group and 12.9% in the prospective one. The analysis of this index of nutrition status also shows the increase in number of overweight children in later study [10].

The anthropometric measurement of skinfolds thickness indicated more patients with outcomes over 90 percentiles than parameters based on the muscles component of body at every stage of treatment, which is coherent to the previous studies in the 80s and which confirm the observation that reserves of fat tissue rebuild faster than proteins [11].

Less children with height index over 90 percentiles during the following assessment provides the height decline during the chronic disease and its treatment.

In our own study we observed a surprisingly large group of children with lower level of HDL fraction and higher level of triglycerides. These abnormal results appeared also at the examination at the end of the treatment with similar frequency. Similar lipids disorders occurred in study done in pediatric oncology patients in the 80s [11]. Twenty years later, in study published in 2008 and done among a group of 25 children with acute lymphoblastic leukemia also indicated the lower level of cholesterol HDL and higher level of triglycerides before the treatment in comparison to the population of healthy children. No correlation between the concentration of lipids and BMI was found [12]. In our own study, the atherosclerotic lipids disorder did not coexist with BMI over 90 percentiles in most cases. Potentially atherosclerotic lipids profile in a quite big group of children discovered at diagnosis confirms the correlation between the lipids disorder and cancer disease, especially they did not meet the criteria of congenital hyperlipidemia. Results of studies suggest

starting the pharmacological treatment in congenital hyperlipidemia to reduce the risk of future cardio-vascular events [7]. In our population of patients abnormal lipid profile was secondary, thus pharmacological treatment was not started. Moreover, statin treatment may be responsible for increased risk of chronic diseases such as diabetes [13]. Tan SY et al. concluded that the prevalence of being overweight and obesity in children with acute leukemia was higher despite lower energy intake compared to controls. Studies assessing physical activity, the complex interaction and the effects of treatment drugs are warranted to better manage malnutrition among pediatric patients [14]. Esbenshade AJ et al. in a prospective cohort of 34 pediatric acute lymphoblastic leukemia (ALL) patients, followed over the first 12 months of ALL maintenance, evaluated changes in body mass index, blood pressure, fasting insulin and glucose, lipids, Homeostatic Metabolic Assessment (HOMA), leptin, and adiponectin. Author found that in these patients over the first year of ALL maintenance therapy demonstrated that components of the metabolic syndrome significantly worsen over time. Preventive interventions limiting increases in BMI and insulin resistance during maintenance therapy should be targeted during this time period to avoid long-term morbidity associated with the metabolic syndrome in long-term survivors [15]. Al-Tawil MM et al. described the studies associating chronic hepatitis C virus (HCV) infection with lipid profile and hepatic steatosis in leukemia or lymphoma cured children. Authors found that serum lipids were low or normal but unfortunately hepatic steatosis was found in a significant proportion of patients and was associated with a poor response to antiviral treatment [16].

The existence of these disorders after the intensive oncological treatment may indicate the negative effect of oncological treatment which may intensify and consolidate the abnormal lipids profile. Children with acute lymphoblastic leukemia administrated glicocortycosteroids and L-Asparaginase, with known negative impact on lipid parameters are in the group of increased risk of these disorders. Reports on potential correlation between hypertriglycerides and thromboembolic complications and pancreatitis require a specially monitoring lipids disorder in this group of patients during the treatment [12].

CONCLUSION

The growing problem of obesity in healthy children in the recent decades concerns also the population of oncological children. They require a special attention and monitoring for negative impact on the development of cardiovascular diseases and diabetes.

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